

We Claim:

Ma Gi F

1. A composition comprising a submicron oilin-water emulsion, and a selected antigen entrapped in, or adsorbed to, a biodegradable microparticle.

- 2. The composition of claim 1, wherein the microparticle is formed from a poly(α -hydroxy acid) selected from the group consisting of poly(L-lactide), poly(D,L-lactide) and poly(D,L-lactide-co-glycolide).
- 3. The composition of claim 2, wherein the microparticle is formed from poly(D,L-lactide-coglycolide.

15

10

4. The composition of claim 1, wherein the submicron oil-in-water emulsion comprises 4-5% w/v squalene, 0.25-0.5% w/v Tween 80®, and 0.5% w/v Span 85®, and optionally, N-acetylmuramyl-L-alanyl-D-isogluatminyl-L-alanine-2-(1'2'-dipalmitoyl-sn-glycero-3-huydroxyphosphoryloxy)-ethylamine.

20

The composition of claim 1, wherein the selected antigen is a viral antigen.

25

- 6. The composition of claim 5, wherein the selected antigen is gplog.
- 7. The composition of claim 5, wherein the 30 / selected antigen is p24gag.
 - ω_{β} . The composition of claim 5, wherein the selected antigen is hepatitis C virus E2.

- 7 %. The composition of claim 1, wherein the selected antigen is entrapped in the microparticle.
- 8 10. The composition of claim 1, wherein the selected antigen is adsorbed to the microparticle.
 - 11. A composition comprising (a) a submicron oil-in-water emulsion which comprises 4-5% w/v squalene, 0.25-0.5% w/v Tween 80®, and 0.5% w/v Span 85®, and optionally, N-acetylmuramyl-L-alanyl-D-isogluatminyl-L-alanine-2-(l'-2'-dipalmitoyl-sn-glycero-3-huydroxyphosphoryloxy)-ethylamine, and (b) a selected antigen entrapped in, or adsorbed to, a poly(D,L-lactide-co-glycolide microparticle.

10 1/2. The composition of claim 1/4, wherein the selected antigen is entrapped in the microparticle.

The composition of claim 1/1, wherein the selected antigen is adsorbed to the microparticle.

14. A method of immunization which comprises administering to a vertebrate subject (a) a submicron oil-in-water emulsion, and (b) a therapeutically effective amount of a selected antigen entrapped in, or adsorbed to, a biodegradable microparticle.

15. The method of claim 14, wherein the microparticle is formed from a poly(α-hydroxy acid) selected from the group consisting of poly(L-lactide), poly(D,L-lactide) and poly(D,L-lactide-co-glycolide).

16. The method of claim 15, wherein the microparticle is formed from poly(D,L-lactide-coglycolide.

M 42

3

5

- 17. The method of claim 14, wherein the submicron oil-in-water emulsion comprises 4-5% w/v squalene, 0.25-0.5% w/v Tween 80®, and 0.5% w/v Span 85®, and optionally, N-acetylmuramyl-L-alanyl-D-isogluatminyl-L-alanine-2-(1'-2'-dipalmitoyl-sn-glycero-3-huydroxyphosphoryloxy) ethylamine.
- 18. The method of claim 14, wherein the selected antigen is a viral antigen.
 - 19. The method of claim 18, wherein the selected antigen is gp 20.
- 15 20. The method of claim 18, wherein the selected antigen is p24gag.
 - 21. The method of claim 18, wherein the selected antigen is hepatitis C virus E2.
 - 22. The method of claim 14, wherein the selected antigen is entrapped in the microparticle.
- 23. The method of claim 14, wherein the selected antigen is adsorbed to the microparticle.
 - 24. The method of claim 14, wherein the submicron oil-in-water emulsion is administered prior to the microparticle.
 - 25. The method of claim 14, wherein the submicron oil-in-water emulsion is administered subsequent to the microparticle.

35

30

	26.	The	meth	nod	oŧ	cla	aim	14,	wherein	the
submicron										
substantia	ally	conci	ırrer	nt/ly	<u>,</u> ψ:	th	the	e mio	croparti	cle.

- 27. A method of immunization which comprises administering to a vertebrate subject the composition of claim 11.
- 28. A method of making a composition

 10 comprising combining a submicron oil-in-water emulsion with a selected antigen entrapped in, or adsorbed to, a biodegradable microparticle.
- 13. The method of claim 2/8, wherein the selected antigen is entrapped in the microparticle.
 - The method of claim 2%, wherein the selected antigen is adsorbed to the microparticle.

25

20

30

35